PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 163734.7 DAB	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IL2005/001280	International filing date *(day/month/year)* 30.11.2005	Priority date *(day/month/year)* 02.12.2004
International Patent Classification (IPC) or national classification and IPC INV. A61P29/00		
Applicant CAN-FITE BIOPHARMA LTD. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.09.2006	26.02.2007
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Rosin, Oliver Telephone No. +31 70 340-8925

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IL2005/001280

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-23 as originally filed

   Claims, Numbers

   1-9 filed with telefax on 31.01.2007

   Drawings, Sheets

   1/2, 2/2 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-9
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The document D1 is regarded as being the closest prior art to the subject-matter of claims 1 and 4 and discloses (the references in parentheses applying to this document) the use of methotrexate (MTX) and the adenosine receptor agonist IB-MECA as single agent medicaments in the treatment of arthritis.

The subject-matter of claims 1 and 4 differs from this known in D1 in that both drugs are used in a combined treatment.

The subject-matter of the independent claims 1 and 4 is therefore new (Article 33(2) PCT).

The problem to be solved by the present invention may be regarded as "how to provide a different use of MTX and IB-MECA".

The solution to this problem proposed in claim "combine both substances" of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
Although D1 discloses the use of either MTX or IB-MECA in the treatment of arthritis, it was not expected that a combination of both drugs would result in an inhibitory effect which is greater than any of the effects of both drugs alone.

Claims 2-3 and 5-9 resp. are dependent on claims 1 and/or 4 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

Claims 1-9 are industrial applicable.

CLAIMS:

1. Use of an A_3 adenosine receptor (A_3AR) agonist for the preparation of a pharmaceutical composition for treating an inflammatory condition which is to be treated with methotrexate (MTX).

2. Use according to Claim 1, for the preparation of a pharmaceutical composition for treating an inflammatory condition which is to be treated with once weekly MTX administration.

3. Use according to Claim 1 or 2, for the preparation of a pharmaceutical composition for 1 to several times daily administrations.

4. Use of MTX for the preparation of a pharmaceutical composition for treating an inflammatory condition which is to be treated with an A_3AR agonist.

5. Use according to Claim 4, for the preparation of a pharmaceutical composition for once weekly administration.

6. Use according to Claim 4 or 5, for the preparation of a pharmaceutical composition for treating an inflammatory condition which is to be treated between 1 and several times daily with said agonist.

7. Use according to any one of Claims 1 to 6, wherein said inflammatory condition is an autoimmune disorder.

8. Use according to Claim 7, wherein said autoimmune disorder is rheumatoid arthritis.

9. Use according to any one of Claims 1 to 8, wherein said A_3AR agonist is IB-MECA.